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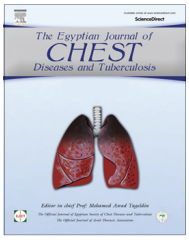

ORIGINAL ARTICLE

Pattern of treatment and clinico-epidemiological analysis of 804 lung and pleura cancer patients treated in radiation oncology department, NCI-Egypt

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KEYWORDS

Lung cancer;
Mesothelioma;
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Abstract *Background:* Epidemiological profile and treatment outcomes of Lung and pleural malignancies vary among different geographical regions. The aim of the study is to analyze the clinico-pathological profile and pattern of treatment of lung and pleural cancers at the Radiation Oncology department, NCI, Cairo University.

Materials and methods: A review of 804 clinical patient records with 770 pathologically/cytologically confirmed patients from Jan 2008-December 2012 was performed. Patients were evaluated (clinical, demographic and pathological profiles) in addition to the treatment adopted.

Results: Median age was 56 years with a male: female ratio of 4:1. Smoking was reported in 63% of patients. Dyspnea and chest pain were the most presenting symptoms (53%). Among lung cancer patients; 78% were NSCLC and 12% SCLC with mesothelioma comprising 10%. Among NSCLCs, adenocarcinoma and large cell undifferentiated carcinoma were the commonest histological subtype (72%). Among NSCLC, 58% cases were of stage IV while among SCLC 73% cases had extensive stage disease. Chemotherapy was administered to 47% (55% vs. 67%, and 35% vs. 31% among non-metastatic lung cancer, mesothelioma patients and metastatic lung cancer and mesothelioma patients respectively). Distant metastases (brain 48%, bone 36%) were reported in 45% of patients. The pattern of treatment intent was palliative (88%) vs. 12% treated with radical intent.

Conclusions: Advanced stages at presentation reflect the palliative pattern of treatment. Hypo-fractionated radiotherapy for lung and pleura malignancies as a palliative measure is

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the current practice. Implementation of early palliative care should be considered for metastatic patients.

Introduction

Lung cancer is the most lethal newly diagnosed cancer. Its high mortality and low 5 years survival rates (< 14%) pose a major challenge in addition to the sharp rise in its incidence among all age groups. The reported median age of lung cancer patients is 65–70 years [1–4]. Untreated lung cancer patients live on an average for 7 months [5].

Estimated new cancer cases of lung cancer is estimated to be approximately 15% among males and 14% among females; ranking second after prostate and breast for both genders; while ranking first for estimated new cancer deaths with a 31% and 26% death rates among males and females respectively [6].

In Egypt, according to the Gharbia population based and National Cancer Institute; Cairo University cancer registries lung cancer ranks 5th and 7th among both genders with a 5% and 4% incidence respectively. Pleural malignancy constitutes 1.4% ranking 16th [7,8].

Tobacco smoking (cigarette); the leading cause for lung cancer, is responsible for about 83% and 90% of females and males lung cancer, respectively. Passive-smokers are also at increased risk of developing lung cancer [4]. Heavy smoking (> 20 cigarettes/day) has been shown to confer a risk of between 15- and 25-fold relative to nonsmokers [9,10].

Lung cancer is pathologically classified into SCLC (15%) and NSCLC types (> 85%). Two thirds of NSCLC have non-resectable disease on initial presentation and less than one third of patients with SCLC have limited-stage disease at presentation. Reported survival rates are commonly very poor even in patients with non-metastatic disease [11–13].

Symptomatic lung cancer patients often presents in a locally advanced or metastatic disease status [14]. Depending on the stage of the disease, therapy is planned with treatment intents either to palliate specific tumor-related symptoms (pain medications/low dose radiotherapy) or local tumor control by trimodality therapy or combinedchemoradiation [15].

Patients presenting with locally advanced or metastatic lung cancer are best treated with palliative-intent radiotherapy (RT); known to be effective in alleviating symptoms resulting from intrathoracic disease, such as hemoptysis, cough, chest pain, dyspnea, and airway obstruction. Short RT fractionation schedules have been recommended by many guidelines [16–21]. The estimated prognosis after diagnosis of advanced disease stage has been reported to be less than 1 year [22,23].

Brain metastasis is reported to be 30–60% among patients diagnosed with lung cancers. Whole brain radiation therapy (WBRT) alone was offered as first-line therapy for the management of brain metastases with reported median survival of 5–6 months [24,25].

Mesothelioma was described as an insidious neoplasm with long latency period (up to 40 years) after exposure to asbestos. Concomitant smoking enhances the risk of malignancy in an asbestos worker, with a 60-fold increased risk of developing NSCLC. Males were three times more likely to be diagnosed than females, and more than half of the patients presented with stage III or stage IV disease [26]. Peak incidence occurs in the 5th and 6th decades of life. Surveillance Epidemiology and End Results (SEER) registry data report approximately 3300 new cases annually, compared to nearly 200,000 cases of lung cancer [27].

Radiotherapy alleviating pain or reducing transient chest wall masses; which has seldom demonstrated significant response as the primary modality for intrathoracic disease did not improve survival [28]. The value of RT in patients with unresectable mesothelioma is controversial, with little evidence supporting RT in the management of mesothelioma [29] Expected median survival in patients treated with chemotherapy is 12 months; and approximately 17 months after administering chemotherapy and RT after Extra Pleural Pneumonectomy [30].

Materials and methods

A retrospective review of lung and pleural cancer patients (N = 804) from the database of the Department of Radiation Oncology – NCI, Cairo University who were treated from January, 2008 through December, 2012; aiming to identify pattern of treatment and analyze their clinical and epidemiological characteristics was performed.

Parameters reviewed in the patients' clinical records included demographic data, presenting symptoms, complete history and physical examination, routine laboratory results, histocytopathological reports, and CT scan of the chest, abdomen, and pelvis; in addition to the treatment adopted. After reviewing patients' records some data were missing due to limitations in the context of the nature imposed by the retrospective study. Most of the patients were treated as a free section with only 27% being referred from insurance hospitals for radiotherapy.

Brain CT/MRI was routinely done at our institution for patients with neurological symptoms or signs. A histological diagnosis of non-small/small cell lung carcinoma was required for treatment unless metastatic disease was evident in the presence of a lung mass upon presentation in a patient with poor performance; therein treatment was started on palliative basis to control symptoms and sputum cytology was requested to reach a diagnosis.

Most of the patients were treated by multidisciplinary approach (free section patients) while those referred from Insurance hospitals; mostly were referred for radiotherapy due to the deficiency of Radiation therapy facility. Treatment protocols included neoadjuvant chemotherapy followed by RT for medically fit patients, while palliative chemotherapy and RT were adopted for medically unfit or patients presented with extra thoracic metastases with poor performance (Appendix 1).

Non-metastatic lung cancer patients were treated by chemo-radiotherapy. Radical RT implemented for curative treatment of patients with un-resectable NSCLC was a 60 Gy total dose and fractionation of 1.8–2.0 Gy per fraction, with one fraction per day, 5 days a week.

Metastatic patients to the brain were treated by palliative whole brain RT a dose of either 30 Gy in 10 fractions over 2 weeks or 20 Gy in 5 fractions over one week depending on the performance status with the shorter regimen being adopted for the poor performance ones.

Single fraction palliative radiotherapy to the bony metastatic sites was the most commonly used fractionation schedule followed by 20 Gy in four or five fractions in one week treatment.

Mesothelioma patients were mainly treated with a palliative intent (30 Gy/10 fractions in 2 weeks) as most patients presented with advanced disease and were considered unrespectable with only 9 patients treated post-operatively. Sixteen patients were treated with a radical dose of 50 Gy/25 fractions in 5 weeks post upfront chemotherapy with stable disease using mixed photon/electron two dimensional radiotherapy; with lung shield and electron beam RT to the pleural surface to avoid radiation pneumonitis.

Ethical consideration

To ensure privacy, dignity and integrity, names of the patient were kept confidential.

Statistical analysis

Data were collected, coded and entered to a computer before being analyzed using the software, Statistical Package for Social Science, (SPSS) version 19. Qualitative data were presented as frequency distribution with its percentage, while quantitative data were presented as means and standard deviation. Comparisons of qualitative data were performed using Chi-squared test while Student's *t*-test was used to compare quantitative data. ANOVA was done whenever needed. *P*-values of <0.05 were considered the cut off point for the level of significance.

Results

Lung cancer was prevalent among males (81.6%) with a male:female ratio of 4:1. Fifty-five percent of the studied patients were <60 years of age and nearly two-thirds lived in urban areas.

Performance status (2) was prevalent (54%) among the studied group compared to 26% with PS 3, 10% with PS 4 and only 10% were PS 1 (Appendix 1). Tobacco smoking was reported in 63%. Most of them were married (98%). Housewives and retired patients were reported to be 17% and 29% respectively, while those with no occupation constituted 11%. Most of the cases were symptomatic, with 26%, 23.5%, 15%, and 11% complained of chest pain, dyspnea, cough and neurological manifestations respectively. Superior Vena Cava obstruction was present in 2% of lung cancer patients. Pleural effusion was present in 28%. Hypertension and diabetes were reported among 12% and 16% respectively. Peak incidence was observed in the year 2012 (Table 1, Fig. 1).

Twenty-four lung cancer patients with Poor performance Status (PS 3 and 4) were diagnosed and treated based on only radiological findings of lung mass with brain and/or bone metastases. In addition ten mesothelioma patients were diagnosed by radiological findings.

Table 1 Patient's demographics.

Items	No. (%)
Gender	
Males	656 (81.6)
Females	148 (18.4)
Age (years) median (56 years)	
⩽40	49 (6.2)
40–60	386 (48.6)
>60	359 (45.2)
Region	
Cairo	579 (72.0)
Upper Egypt	145 (18.0)
Lower Egypt	80 (10.0)
Occupation	
Workers	112 (16.0)
Farmers	48 (6.0)
Employees	66 (8.1)
Driver	41 (5.0)
Carpenter	10 (1.2)
No occupation	405 (49.0)
Others	26 (3.2)
Symptoms	
Cough	122 (15.2)
Dyspnea	189 (23.5)
Chest pain	215 (26.2)
Hemoptysis	81 (10.1)
Hoarseness of voice	7 (9.0)
Neurological manifestation	90 (11.2)
Bone pains	67 (8.3)
Superior Vena Cava obstruction	15 (1.9)
Family history	
Yes	29 (3.6)
No	715 (89.0)
Smoking	
Yes	477 (63.0)
No	281 (37.0)

Some clinical records were deficient significance is that if you add the numbers it will not show the 100% of the studied population.

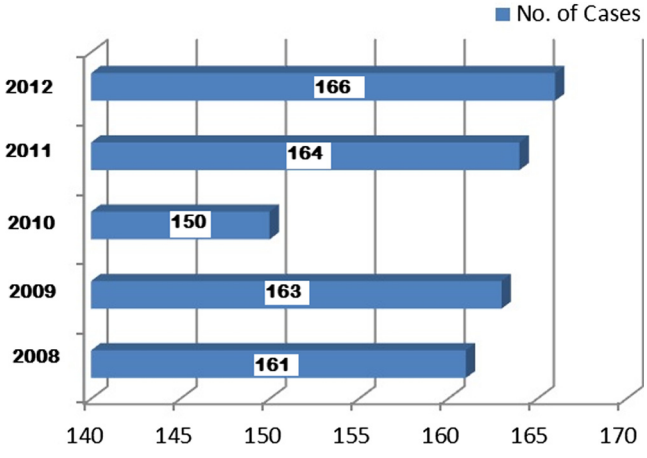

Figure 1 Frequency of cases over the studied 5 years.

Non-small cell lung carcinoma pathology was reported in (79%) compared to 12% for small cell carcinoma pathology. Only 6% of NSCLC underwent curative surgery. Regarding radiation therapy treatment, most of the cases (88%) were treated with a palliative intent compared to only (12%) for whom radical radiotherapy was adopted. Radiotherapy to primary site with a radical intent was reported in 19%, 5% and 3% for NSCLC, SCLC and mesothelioma patients respectively (Fig. 2).

The below Fig. 3 shows the yearly distribution of pathologically proven referred cases for treatment in the radiotherapy department which showed a statistical significance between the three types of pathology ($p = 0.001$).

Tables 2 and 3 showed statistical significance difference comparing disease pathology and disease status (localized/metastatic) with chemotherapy treatment, smoking, gender, age, occupation, and disease symptoms.

Chemotherapy was implemented in 55% and 67% among the non-metastatic lung cancer and mesothelioma patients respectively; while only 35% and 31% of metastatic lung cancer and mesothelioma patients were treated by palliative chemotherapy. Among the whole group of the studied patients 53% were not treated by chemotherapy compared to 47% treated by chemotherapy.

Metastatic disease at presentation was reported in 45% of patients; brain as the only site of metastases was reported among 46% followed by bone only metastasis in 36% of the treated patients (Table 4).

Discussion

Analysis of the clinico-pathological profile of lung and pleura cancer patients at our department as compared to Western population revealed that median age (56 years) of our patients was almost 10 years younger [31–33]; with most of the previous Egyptian studies reporting a similar (5th decade) median age [34–36]. Smoking is always attributed to lung cancer development [37,38]. In this study, almost two/third of the patients were smokers; most of which were cigarette smokers. Smoking was prevalent mainly in the urban population.

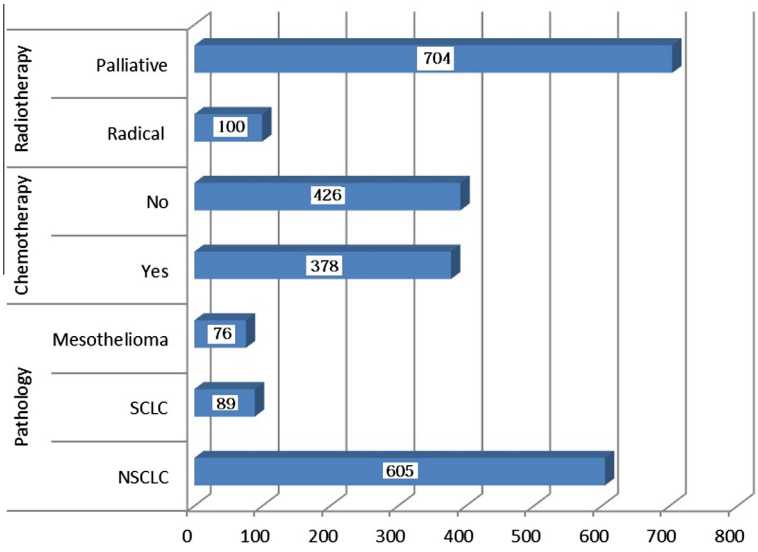

Figure 2 Distribution of patients in relation to pathology and pattern of Radiotherapy treatment.

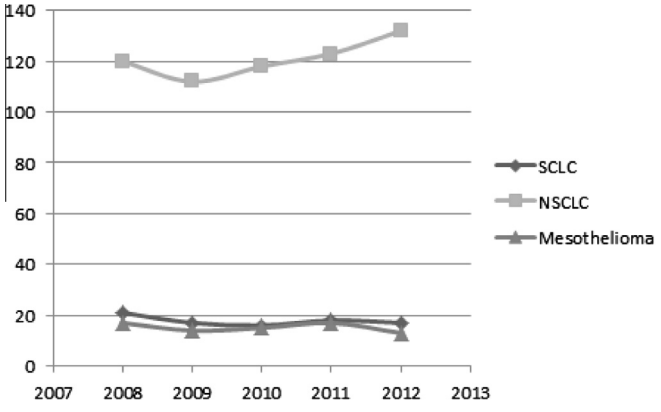

Figure 3 Distribution of the studied population according to disease pathology.

Table 2 Pathology versus patients characteristics.

Variable		Pathology			Total	*P*-value
		SCLC	NSCLC	Mesothelioma		
Chemotherapy**	No	35	329	36	400	0.021
	Yes	54	276	40	370	
Smoking	No	13	206	66	285	0.001
	Yes	76	399	10	485	
Gender	Female	12	99	31	142	0.001
	Male	77	506	45	628	
Age	< 40	5	27	15	47	0.001
	41–60	41	270	56	367	
	> 61	21	303	15	339	
Governorate	Giza, Cairo, Qalyoubia	58	409	49	516	0.002
	Minia, Fayoum, Beni-Suef	11	101	12	124	
	Helwan	3	28	10	41	
	Delta	17	44	3	64	
	Assuit, Sohag, Qena, Aswan	0	12	2	14	
	Suiz, Ismailia	0	11	0	11	
Occupation	Workers	28	93	6		0.0001
	Farmers	4	35	7		
	Retirement	17	165	13		
	Employees	8	39	12		
	Housewives	6	91	22		
	None	6	58	9		
	Driver	7	31	3		
	Carpenter	0	9	1		
	Others*	9	14	3		
Symptoms	Cough	21	83	13		0.0001
	Dyspnea	11	140	21		
	Chest pain	22	149	32		
	Hemoptysis	1	75	2		
	Hoarseness of voice	2	4	0		
	Neurological manifestation	5	80	2		
	Bone pains	8	51	5		
	Superior Vena Cava Obstruction	4	11	0		

* Others: butcher, baker, plumber.
** Thirty-four patients were treated with palliative RT only.

Table 3 Relationship between disease status and smoking, gender, age group and chemotherapy.

Variable		Diseases				Total	*P*-value
		Lung cancer	Mesothelioma	Metastatic lung cancer	Metastatic mesothelioma		
Chemotherapy	No	166	22	227	11	426	0.001
	Yes	204	48	121	5	378	
Smoking	No	86	48	131	16	281	0.001
	Yes	246	16	215	0	477	
Gender	Male	335	57	259	5	656	0.001
	Female	35	24	71	18	148	
Age	< 40	22	11	11	5	49	0.001
	41–60	137	52	183	14	386	
	> 61	206	17	132	4	359	

Advanced disease (stage IIIB–IV) at the time of presentation was (70% in NSCLC and 71% in SCLC); similar to others from national and western series with almost 2/3 of patients of NSCLC and of SCLC present in advanced stage [39–42].

Although the use of palliative chemotherapy for NSCLC is increasing, RT alone can provide more timely palliation of thoracic symptoms without the morbidity of chemotherapy, and may be the primary or only treatment option for

Table 4 Distribution of disease status among the studied population.

Disease status	Percentage (%)
Non-metastatic lung cancer	370 (51.6%)
Total metastatic lung cancer	348 (48.4%)
• Metastatic LC to lungs	• 30 (8.6)
• Metastatic LC to brain	• 166 (47.7)
• Metastatic LC to bone	• 124 (35.6)
• Metastatic LC to liver	• 17 (5.0)
• Metastatic LC to bone and liver	• 11 (3.1)
Non-metastatic mesothelioma	70 (79.0%)
Total metastatic mesothelioma	16 (21.0%)
• Metastatic mesothelioma to lungs	• 5 (31.0)
• Metastatic mesothelioma to brain	• 2 (12.5)
• Metastatic mesothelioma to bone	• 7 (44.0)
• Metastatic mesothelioma to liver	• 2 (12.5)
Total	804 (100%)

poor-PS patients, or patients who have declined or progressed despite systemic therapy.

Analysis of the pattern of treatment in the current study revealed that 53% of the studied patients were not treated by chemotherapy (54% of NSCLC, 39% of SCLC and 47% for mesothelioma) and only 35% and 31% of metastatic lung cancer and mesothelioma patients were treated by palliative chemotherapy. These figures are higher than those reported (20–37%) in USA, Scotland and Australia (19–30% of NSCLC and 20–25% of SCLC) and similar (43–50%) to reports from Ireland, New Zealand and India [41,43–48]; factors that might be attributed for these differences were poor PS, advanced disease stages and social reasons.

Radiotherapy in radical doses to the primary site with a radical intent was adopted in only 19%, 5% and 3% of NSCLC, SCLC and mesothelioma patients; findings that are inferior to the reported figures (29–42% of NSCLC and 27–36% of SCLC) received radical radiotherapy [11,49–50]. In actual practice, 36–65% of non-metastatic cases actually receive radiotherapy despite that guidelines recommend that up to 76% of lung cancer patients should receive radiotherapy during their treatment [51]. Palliative radiotherapy; the most common type (88%) for local lung symptom control or for brain and bone metastases adopted among the studied population was in concordance with the internationally published guidelines [17–21]. The marked underutilization radical radiotherapy as a treatment modality may be explained by the still practice of systemic chemotherapy for patients away from a Radiotherapy facility. Outcome of these patients still remains poor because of late presentation in advanced stage and poor PS with many of them not amenable for radical, aggressive treatment.

Conclusions

This 5-year analysis confers the predominance of late advanced stages at presentation in addition to the high percentage of metastatic patients reflecting the palliative pattern of treatment. Hypo-fractionated Radiotherapy for lung and pleura malignancies as a palliative measure is the current practice. National awareness campaigns are important to be implemented in an effort to combat smoking (active/passive) and to ensure industrial safety measures against asbestos and chemical industrial aerosols as the only important preventive measure. Early implementation of palliative care may lead to significant improvements in quality of life for patients with poor prognosis.

Conflict of interest

Authors declare no conflict of interests exists and no financial or non-financial interest to be disclosed.

Appendix 1

Eastern Cooperative Oncologic Group (ECOG) performance status.

Grade	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

Oken MM, Creech RH, Tormey DC, et al. (1982). "Toxicity and response criteria of the Eastern Cooperative Oncology Group". Am. J. Clin. Oncol. 5 (6): 649–55.

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